ST1 type; and in-turn evolved recently to become the "epidemic" ST7 type. The virulence increased in the ST7 type with its ability to stimulate massive amounts of pro-inflammatory cytokines that led to the Streptococcal toxic shock like syndrome.
Based on the information generated, we proposed a two stage theory for the pathogenic mechanism of S. *suis*. When the pathogen enters the human body (bloodstream), stage one is initiated showing communication between bacterial cell wall components with the host immune system using pattern recognition receptors such as Toll-like receptor 2 and CD14; and probably by using the two-component signal transduction system acquired recently with the consequent burst of pro-inflammatory cytokines. The ST7 S. *suis* would have mutated to stimulate the host to produce massive amount of cytokines such as TNF-α, IL-1β and interferon gamma that regulate high production levels of other cytokines such as IL-6 and IL-12, leading to the STSLS. If a patient survives the first stage, the pathogen may reach the central nervous system traveling free in the circulation or monoctye-associated to cause the meningitis. The clinical significance of these findings was to prevent sudden death associated with ST7 or ST1 S. *suis* infections where the treatment was initiated early during the acute phase of the infection, specially for therapies to prevent or reduce the risk of STSLS.

Concurrent Session 3 – HIV – Overview

I-21 Prevalence of drug resistant HIV-1 in rural areas of Hubei province in the People's Republic of China

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Objective: To determine the prevalence of drug resistant HIV-1 and the efficacy of first-line HAART regimens consisting of generic NRTI and NNRTI among 339 study subjects in rural areas of Hubei province, China.
Methods: Two cross-sectional studies were conducted to investigate 150 HAART-naive (99 received subsequent therapy) between 2003 and 2005 and 288 HAART-experienced patients between 2006 and 2007. Patients' $CD4^+$ T-cell count and viral load were determined. HIV-1 *pol* gene fragments were amplified from patients' plasma by RT-PCR, subsequently sequenced and analyzed.
Results: 83.5% of the patients were from rural villages. They were dominantly infected with subtype B′ HIV-1 (97.4%) through paid blood donation (64.6%) and related blood transfusion (28.3%). We found that there was a steady increase of CD4 count over time among treated patients without detectable viral load (186/288, 64.6%). There was, however, an increasing prevalence of NRTI and NNRTI resistant mutations among patients with detected viremia (102/288, 35.4%) after treatment for 3–6 (24.3%), 9–12 (57.1%) and 20–24 (63.3%) months, respectively. The increasing rates were associated with significant CD4 count drop and viral load increase. Some patients also developed multi-drug resistant mutants.
Conclusions: We report the first HIV-1 drug resistance study after two-years on HAART among Chinese patients living in rural villages. Our data suggest that a significant portion of patients are failing first-line regimens with a trend of AIDS progression. It is therefore necessary to maximize the drug adherence and to make affordable second-line HAART regimens available immediately. Our results have implications for implementing HAART in under-resourced developing country settings.

I-22 Molecular epidemiology of drug resistant HIV-1 in Hong Kong

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The combination antiretroviral therapy is referred as Highly Active Antiretroviral Therapy (HAART) which inhibits different pathways of HIV pathogenesis so that viral replication can be effectively suppressed. Following the introduction of HAART since late 90s, significant decline in morbidity, mortality and HIV/AIDS incidence was reported in Hong Kong. To monitor the efficacy of HAART, genotyping resistance test (GRT) by PCR-sequencing of the viral *pol* gene (PR codon 1 to RT codon 410) was used to study 1,015 samples collected from 830 HIV-1+ patients. Results showed good concordance to clinical response among treatment experienced patients. Primary resistance was detected among 6.7% of the treatment naive samples and GRT also revealed the predominant subtypes CRF01_AE (45.8%) and B (41.2%) were followed by C (4.4%), CRF07_BC (1.7%), A1 (1.3%), CRF08_BC (0.9%), CRF02_AG (0.6%), CRF06_cpx (0.3%) and G (0.1%). Mutations D30N, G48V and I84V were only detected in subtype B while V32I mutation was only detected in CRF01_AE. Resistance associated with HAART were detected among 10% treatment experienced patients after 18–24 months on HAART in Hong Kong. Increasing prevalence of the primary resistance in Hong Kong was detected since 1997 without subtype preference. The presence of primary resistance in treatment naive patients indicates the need for GRT on pre- and post-treatment samples, so that appropriate regimens for HAART can be implemented. Phylogenetic analysis of the *pol* gene also identified 3 major local clusters of CRF01_AE subtypes and B subtypes which were clonally related to reference sequences from major cities in China (Fujian, Pingxiang and Nanning).

I-23 Opportunistic infections in AIDS: Thai experience

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The first Thai AIDS case was imported in 1984, since then approximately one million Thais have been infected with HIV, and currently, the estimated prevalence of HIV infection is about 1%. There were 5 consecutive epidemic waves as follows: among male homosexuals (started 1985), rapid surge in intravenous drug users (1988), followed by female commercial sex workers (1989), their male clients (1990) and lastly wives and newborn of the latter (1991). Most HIV infection is transmitted via heterosexual activities. This spreading of infection occurred rapidly and caused great alarm to all people involved.
Fortunately, the Thai Government at that time has recognized this problem and considered AIDS prevention and control a high national priority, involving several ministries: Education, Health, Interior, etc. Thailand has successfully slowed down the epidemic. However, hundred thousands of people have already been infected. Prior to the HAART era, hundreds of HIV-infected people became ill with opportunistic infections (OI) and hence the diagnosis of AIDS with high mortality. From our experience during

1990–94, after the diagnosis of OI, one-year survival probability is only 59.8% (95% CI 52.0–67.7%). The most common OI's are tuberculosis (40–50%), cryptococcosis (25–40%), *Pneumocystis carinii* pneumonia PCP (10–20%), toxoplasmosis (5–10%) and salmonellosis (5–10%). In the northern part of Thailand, where *Penicillium marneffei* is endemic, this infection is as common as tuberculosis, indicating the importance of local endemic infection to be recognized as AIDS-defining illnesses. Cryptococcosis carries the worst prognosis with 1-year survival probability of 31.9% (16.8–48.1%).

Since HAART became available and financially supported by Thai Government in 2001, the morbidity and mortality of HIV-infected persons have decreased remarkably. OI's has decreased and people living with AIDS/HIV survive much longer. The emergence of drug-resistant HIV has posed problems since the second line drugs are much more expensive and not many to choose from. In addition, this group can transmit drug-resistant HIV causing primary drug-resistant HIV infection which will make it more difficult to choose the proper regimen without genotyping the virus. Thus, strong prevention and control program should remain at top priority, to stop new infection and transmission.

I-24 HIV-specific T-cell responses in a cohort of slow progressors in China

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Background: There is an urgent need for an effective vaccine to prevent HIV-1 infection, and current efforts are directed towards generating vaccine candidates that will elicit a T-cell immune response to the virus.. No studies to date have described mechanisms of HIV resistance or delayed disease progression in Chinese cohorts. For both the design and the evaluation of CTL-inducing vaccines it is important to define immunodominant CTL epitopes for both the prevailing HLA types and the most common viral strains affecting that population. Morever, it is also important to identify composite features of T-cell responses associated with good outcome and T-cell epitopes that will generate such beneficial features.

Study cohort: Current studies are limited by the facts that most of the study cohort subjects have been infected for different lengths of time; infected with different viral strains and have a diverse genetic background. In this study, we have access to a unique village cohort of patients (N = 407) who were involved in a plasma donation scheme that became contaminated with clade B HIV-1 in the period 1994–1995. 137 premature adult deaths were recorded in the village with symptoms compatible with HIV-1 disease before 2003. Of the surviving patients, none were treated before 2003: therefore the proportion of slow or non-progressors is unusually high in this cohort (>50% had CD4 counts >200 in 2004).

Results: We found that HLA-A30 and B51 were strongly associated with low viral load in this cohort. We investigated the hypothesis that immunodominant T-cell responses to conserved HIV-1 proteins restricted by these alleles could be partially responsible for good control of virus. We used ELISPOT assays to test for responses to overlapping Clade B peptides spanning the whole viral proteome and to the 202 best characterised optimal epitopes from the Los Alamos data base. We found broad T cell responses, especially directed towards the gag protein, in patients with low viral loads. The immunodominance hierarchy of epitopes restricted by common HLA molecules in the cohort showed very different patterns from a published acute cohort (Altfeld, 2006). We have sequenced the gag and nef genes from 97 patients and will present data to show that the loss of certain responses in the chronic phase of infection might be due to early selection of escape mutants.

Conclusion: We have identified a panel of immunodominant T-cell responses restricted by common HLA alleles in a Chinese slow progressor cohort. Identification of the most beneficial responses will be particular important for future vaccine design targeted to the Chinese population.

I-25 Outcomes and challenges of the China National Free Antiretroviral Treatment Program

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To combat the HIV/AIDS epidemic in China, the National Center for AIDS/STD Control and Prevention established the Division of Treatment and Care in late 2001. The pilot for the National Free ART Program began in Henan Province in 2002, and the program fully launched in 2003. Initially, treatment efforts focused on patients infected through illicit blood and plasma donations in the mid-1990s, and subsequently expanded to include HIV-infected injection drug users, commercial sex workers, pregnant women, and children. The National Free ART Database was established in late 2004, and includes data on current patients and those who were treated before 2004. Over 50,000 adult and pediatric patients have been treated thus far. Challenges for the program include integration of drug treatment services with ART, an under-resourced health care system, co-infections, stigma, discrimination, drug resistance, and procurement of second-line ART. The merging of national treatment and care, epidemiologic, and drug resistance databases will be critical for a better understanding of the epidemic, earlier identification of patients requiring ART, and improved patient follow-up. The Free ART Program has made considerable progress in providing the necessary care and treatment for HIV-infected people in China and has strong government support for continued improvement and expansion.

Concurrent Session 4 – Immunology and Virology

I-26 Immunology of HBV infection

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HBV is an enveloped, hepatotrophic, oncogenic hepadnavirus that infects hepatocytes and leukocytes of humans and chimpanzees. The clinicopathological outcomes of HBV infection are determined by both viral and host factors. HBV infects hepatocytes without triggering apoptosis, altering hepatocyte gene expression or inducing innate immune production of IFNα or IFNβ. Host determinants of outcomes are the quality, quantity, kinetics and immunoregulation of the integrated innate and adaptive immune responses. HBV subverts the innate immune response by down-regulating (1) expression of MICA, the primary ligand for the NKG2D receptors of NK cells and (2) TLR1, 2, 4 and 6 transcripts in PBMC. In addition, HBV persistence and disease progression is favored by the low production of mannose binding lectin (MBL) and reduction in the interferon-inducible APOBEC3 family of cytidine deaminases that inhibit HBV replication and hypermutate the HBV genome. Generation of polyclonal, multi-antigen-specific CD4 T-cell and CD8 cytotoxic T lymphocytes (CTL) is required for resolution of acute HBV infection through the combined effects of HBV-specific cytolysis of infected